PATENT COOPERATION TREAL PATENT DEPARTMENT RECEIVED From the INTERNATIONAL SEARCHING AUTHORITY PCT JUN 2 6 2002 To: SCHERING CORPORATION NOT FICATION OF TRANSMITTAL OF Computer Input THE INTERNATIONAL SEARCH REPORT Patent Departement K-6-1 1990 OR THE DECLARATION 2000 Galloping Hill Road Date: Kenilworth, NJ 07033-0530 mic. PA: HHC UNITED STATES OF AMERICA (PCT Rule 44.1) Attny: CHECK FILE T FILE Date of mailing (day/month/year) 07/06/2002 Applicant's or agent's file reference IN01159K FOR FURTHER ACTION See paragraphs 1 and 4 below International application No. International filing date PCT/US 01/22678 (day/month/year) 19/07/2001 **Applicant** SCHERING CORPORATION 1. X The applicant is hereby notified that the International Search Report has been established and is transmitted herewith. Filing of amendments and statement under Article 19: The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46): When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet. Where? Directly to the International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Fascimile No.: (41-22) 740.14.35 For more detailed instructions, see the notes on the accompanying sheet. The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith. With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that: 3. the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices. no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made. 4. Further action(s): The applicant is reminded of the following: Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication. Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later). Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II. Name and mailing address of the International Searching Authority Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Joannes Vergoosen Tel. (+31-70) 340-2040, Tx. 31 651 epo ni,

Fax: (+31-70) 340-3016

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international poulication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been its filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

- [Where originally there were 48 claims and after amendment of some claims there are 51]:
 "Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
- 2. [Where originally there were 15 claims and after amendment of all claims there are 11]: "Claims 1 to 15 replaced by amended claims 1 to 11."
- 3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
 "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
 - "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or "Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
- 4. [Where various kinds of amendments are made]: "Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREAT.

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.			
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)		
PCT/US 01/22678	19/07/2001	21/07/2000		
Applicant		•		
SCHERING CORPORATION				
This International Search Report has bee according to Article 18. A copy is being to	n prepared by this International Searching Aut ansmitted to the International Bureau.	nority and is transmitted to the applicant		
This International Search Report consists It is also accompanied by	of a total of Sheets. If a copy of each prior art document cited in this	report.		
Basis of the report With regard to the language, the	international search was carried out on the ba	sis of the international application in the		
language in which it was filed, un	less otherwise indicated under this item.	••		
the international search v Authority (Rule 23.1(b)).	was carried out on the basis of a translation of	the international application furnished to this		
b. With regard to any nucleotide as		nternational application, the international search		
was carried out on the basis of the contained in the internation	ne sequence listing : onal application in written form.			
	ernational application in computer readable for	m.		
furnished subsequently to	o this Authority in written form.			
	o this Authority in computer readble form.			
the statement that the su	bsequently furnished written sequence listing of as filed has been furnished.	does not go beyond the disclosure in the		
		is identical to the written sequence listing has been		
2. X Certain claims were for	und unsearchable (See Box I).			
3. Unity of invention is lac	cking (see Box II).			
4. With regard to the title ,				
the text is approved as s	submitted by the applicant.			
1	shed by this Authority to read as follows:	ATTTIC C VIDUC		
PEPTIDES AS NS3-SERIN	PROTEASE INHIBITORS OF HEP	AIIIIS C VIKUS		
5. With regard to the abstract,				
	submitted by the applicant.			
the text has been establi	ished, according to Rule 38.2(b), by this Author ne date of mailing of this international search re	rity as it appears in Box III. The applicant may, eport, submit comments to this Authority.		
6. The figure of the drawings to be pul	blished with the abstract is Figure No.			
as suggested by the app	olicant.	X None of the figures.		
because the applicant fa	ailed to suggest a figure.	•		
because this figure bette	er characterizes the invention.			

INTCRNATIONAL SEARCH REPORT

iternational Application No PCT/US 01/22678

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K5/062 C07K5/065

A61K38/05

A61P31/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 01 74768 A (VERTEX PHARMA ;COURT JOHN (US); MALLEY ETHAN O (US); PERNI ROBERT) 11 October 2001 (2001-10-11) claims; examples	1-38
Ρ,Χ	WO 01 40262 A (DU PONT PHARM CO) 7 June 2001 (2001-06-07) claims; examples	1-38
P,X	WO 00 52032 A (DAINIPPON) 8 September 2000 (2000-09-08) & EP 1 157 998 A 28 November 2001 (2001-11-28) claims; examples	1-38

X Further documents are listed in the continuation of box C.	γ Patent family members are listed in annex.
 Special categories of cited documents: A' document defining the general state of the art which is not considered to be of particular relevance E' earlier document but published on or after the international filing date L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) O' document referring to an oral disclosure, use, exhibition or other means P' document published prior to the international filing date but later than the priority date claimed 	 "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
Date of the actual completion of the international search	Date of mailing of the international search report
28 May 2002	07/06/2002
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Fuhr, C

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INTTONAL SEARCH REPORT

nternational Application No
PCT/US 01/22678

····	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	Relevant to claim No.	
Category *	Citation of document, with indication, where appropriate, of the relevant passages		
X	HAN WEI ET AL: "alpha-Ketoamides, alpha-ketoesters and alpha-diketones as HCV NS3 protease inhibitors." BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 10, no. 8, 17 April 2000 (2000-04-17), pages 711-713, XP002199468 ISSN: 0960-894X the whole document	. 1-38	
X	WO 99 07734 A (BAILEY MURRAY DOUGLAS; BOEHRINGER INGELHEIM CA LTD (CA); HALMOS TE) 18 February 1999 (1999-02-18) compounds 103, 109, 112, 115, 116, 225, 227, 229 claims; tables 1,2	1-38	
X	LLINAS-BRUNET MONTSE ET AL: "Studies on the c-terminal of hexapeptide inhibitors of the hepatitis C virus serine protease." BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 8, no. 19, 6 October 1998 (1998-10-06), pages 2719-2724, XP002199470 ISSN: 0960-894X compounds 14 and 18	1-38	
X	WO 98 17679 A (DEININGER DAVID D ;MURCKO MARK A (US); VERTEX PHARMA (US); FARMER) 30 April 1998 (1998-04-30) compound 80 claims	1-38	

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INTF NATIONAL SEARCH REPORT

Information on patent family members

ternational Application No PCT/US 01/22678

		Dublication		Patent family	Publication
Patent document cited in search report		Publication date		member(s)	date
WO 0174768	Α	11-10-2001	AU	5116501 A	15-10-2001 11-10-2001
			WO	0174768 A2	. 11-10-2001
WO 0140262	Α	07-06-2001	AU	2055301 A	12-06-2001
			WO	0140262 A1	07-06-2001
WO 0052032	 A	08-09-2000	JP	2000256396 A	19-09-2000
WO 0032032	••		AU	2690200 A	21-09-2000
			CN	1349542 T	15-05-2002
			EP	1157998 A1	28-11-2001
			MO	0052032 A1	08-09-2000 28-09-2001 -
			NZ	513594 A	21-01-2002
			TR 	200102540 T2	
WO 9907734	Α	18-02-1999	AU	8846698 A	01-03-1999
			WO	9907734 A2	18-02-1999
			EP	1012180 A2	28-06-2000
			HU	0100100 A2	28-11-2001
			JP	2001512744 T	28-08-2001 07-11-2000
			US 	6143715 A	0/-11-2000
WO 9817679	Α	30-04-1998	AP	1019 A	16-10-2001
No solver			AT	212037 T	15-02-2002
			AU	719984 B2	18-05-2000
			AU	5147798 A	15-05-1998 31-01-2000
			BG	103392 A	19-10-1999
			BR	9712544 A 1238780 A	15-12-1999
			CN CZ	9901340 A3	11-08-1999
			DE	69709671 D1	21-02-2002
			DK	932617 T3	22-04-2002
			EE	9900161 A	15-12-1999
			EP	1136498 A1	26-09-2001
			EP	0932617 A1	04-08-1999
			HU	0000152 A2	28-07-2000
			JP	2001502694 T	27-02-2001
			NO	991832 A	17-06-1999
			NZ	335276 A	29-09-2000
			PL	332872 A1	25-10-1999 10-04-2000
			SK	51099 A3	21-10-1999
			TR	9901602 T2 9817679 A1	30-04-1998
			WO US	6265380 B1	24-07-2001
			U3		
			US	2002032175 A1	14-03-2002

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-38 relate to an extremely large number of possible compounds, compositions and methods. In fact, the claims contain so many options and possible permutations that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and/or concise), namely those compounds recited in the examples and in claim 39 and closely related homologous compounds and the compositions and methods relating to them.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

International application No. PCT/US 01/22678

INTERNATIONAL SEARCH REPORT

Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
	Although claims 35 and 36 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. X	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
	see FURTHER INFORMATION sheet PCT/ISA/210
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inte	ernational Searching Authority found multiple inventions in this international application, as follows:
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
з	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remari	k on Protest The additional search fees were accompanied by the applicant's protest.
	No protest accompanied the payment of additional search fees.

PCT

世界知的所有権機関 国際事務局 特許協力条約に基づいて公開された国際出願



(51) 国際特許分類7

C07K 5/103, 5/083, C07D 239/54, 233/34, A61K 38/55, A61P 43/00, 11/00 (11) 国際公開番号

WO00/52032

(43) 国際公開日

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(21) 国際出願番号

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A1

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(30) 優先権データ

特願平11/56052

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(81) 指定国 AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, 欧州特許 (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI特許 (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG), ARIPO特許 (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), ユーラシア特許 (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM)

添付公開書類

国際調査報告書

HETEROCYCLIC COMPOUNDS, INTERMEDIATES THEREOF AND ELASTASE INHIBITORS (54)Title:

(54)発明の名称 複素環式化合物およびその中間体ならびにエラスターゼ阻害剤

$$HOOC_{A} \stackrel{D}{\longrightarrow} B \stackrel{Q}{\longrightarrow} N \stackrel{R^1}{\longrightarrow} N \stackrel{R^2}{\longrightarrow} R^5$$

$$(I-a)$$

(57) Abstract

Heterocyclic compounds represented by general formula (I-a), its esters or salts thereof; and human neutrophilic elastase inhibitors, etc. containing the same as the active ingredient wherein A and B are the same of different and each represents lower alkylene optionally substituted by oxo; D represents a monocyclic or dicyclic heterocyclic group optionally substituted by oxo; R¹ and R² are the same or different and each represents lower alkyl; R3 and R4 are different from each other and each represents hydrogen or hydroxy, or R3 and R4 form together oxo; and R⁵ represents 2-benzoxasolyl, trifluoromethyl, benzylaminocarbonyle, etc.